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Nanoworms Target Tumors

A new shape for nanoparticles helps deliver imaging agents.

By Corinna Wu

Early-stage tumors are often too small to see with magnetic resonance imaging (MRI). Now, a team of researchers has developed magnetic "nanoworm" particles that can circulate for a day in the bloodstream and home in on tumors, helping to enhance an MRI image. The nanoworms could make it easier to image small tumors, allowing cancer to be detected and treated earlier.

The research is part of a broader effort to treat cancer more effectively by delivering drugs and imaging agents directly to diseased cells using nanoparticles. But the challenge has been to create delivery vehicles that will circulate in the body long enough to find their way to a tumor in order to do their job. "You're always fighting a battle with the body's own rejection systems--the natural systems that try to get rid of any foreign body, such as a nanoparticle," says Michael Sailor (http://chem-faculty.ucsd.edu/sailor/people/msailor.html) , a professor of chemistry and biochemistry at the University of California, San Diego.

One option is to chemically treat the nanoparticles so that they're not recognized by the body's immune system. But increasingly, researchers are also tailoring the nanoparticles' shape to help them slip by defenses. The nanoworms created by Sailor and his colleagues consist of spherical iron oxide nanoparticles linked together so that they resemble the segments of an earthworm. The nanoworms are about 30 nanometers in length and are coated with a sugar called dextran that helps them evade the body's rejection system. The shape also helps. Previous studies have shown that particles with an elongated shape are not eaten up by phagocytes, immune cells responsible for clearing such particles from the body, as readily as spherical ones are.

The new study "fits into the emerging evidence in nanomedicine that shape is very important," says Mauro Ferrari, director of the Center for NanoMedicine and chair of the department of biomedical engineering at the University of Texas Health Sciences Center, in Houston. Controlling size and shape is a powerful way of directing drug carriers (http://www.technologyreview.com/Nanotech/20547/) to their intended targets, Ferrari says.

Drugs could be attached to the nanoworms, but their impact will be mostly in their applications to imaging, Sailor says. Sailor, collaborating with Sangeeta Bhatia (http://lmrt.mit.edu/personnel/sangeeta.asp) at MIT and Erkki Ruoslahti (http://www.burnham.org/default.asp?contentID=209) at the University of California, Santa Barbara, reported their findings in the journal *Advanced Materials*.

The synthesis of the nanoworms was somewhat unexpected, Sailor says. By using dextran molecules of slightly different weight, the researchers found that the particles spontaneously aggregated into strings of about eight to ten nanoparticles. Then Ji-Ho Park, a materials-science and engineering graduate student, tested their magnetic properties. Compared with individual iron oxide nanoparticles, the nanoworms produced a massively enhanced MRI signal. "Ultimately, this should lead us to image smaller tumors, so that would be at an earlier stage of development in the body," Sailor says.

When injected into mice, the nanoworms accumulated in tumors, which was not surprising. "When [tumors] recruit blood vessels to feed themselves, the blood vessels tend to be very leaky," Sailor says, so any kind of nanoparticle would have a tendency to collect there. But the nanoworms also stuck around much longer than individual iron oxide nanoparticles, which the body can eliminate in minutes. "If you make [a nanoparticle] bigger, then the body should have a better chance of finding it and eliminating it," Sailor says. "So one of the surprises of the study was that these things would circulate for quite a long time. They had up to a 24-hour half-life."

The researchers also took the nanoworms and attached a peptide called F3, developed by Ruoslahti and his colleagues, that targets the surface of cancer cells. In vitro, the modified nanoworms attached to cancer cells more effectively than individual nanoparticles did. Linking several nanoparticles together creates a cooperative effect, Sailor says. Once one F3 molecule contacts a cell surface, there are others nearby to do the same.

Sailor and his group are now looking at methods to amplify the effect of the nanoworms, finding means for them to recruit other particles to a tumor site in a way that blood might clot.

Upcoming Events

2010 IEEE Conference on Innovative Technologies for an Efficient and Reliable

Electricity Supply (http://www.ieee-energy.org/)
Waltham, Massachusetts
Sunday, September 27, 2009 - Tuesday, September 28, 2010
http://www.ieee-energy.org/ (http://www.ieee-energy.org/)

FutureM (http://www.futurem.org/Default.aspx)
Boston, MA
Monday, October 04, 2010 - Friday, October 08, 2010
http://www.futurem.org/Default.aspx (http://www.futurem.org/Default.aspx)

USA Science & Engineering Festival Expo (http://www.usasciencefestival.org)
Washington, D.C.
Saturday, October 23, 2010 - Friday, October 29, 2010
http://www.usasciencefestival.org (http://www.usasciencefestival.org)

15th Annual MITX Interactive Awards
(http://www.mitxawards.org/interactive/default.aspx)
Boston, Massachusetts
Thursday, November 18, 2010
http://www.mitxawards.org/interactive/default.aspx
(http://www.mitxawards.org/interactive/default.aspx)